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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,965	03/31/2004	Robert Falotico	CRD-5073 NP	7706

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
06/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/813,965	FALOTICO ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/21/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,9 and 10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed March 21, 2007 have been received and entered into the application. Accordingly, claims 2, 6 and 8 are cancelled; claims 1 and 7 are amended. Claims 1, 3-5, 7, 9 and10 are pending among which claims 1, 3-5 and 7 are being examined on the merits. Claims 9 and 10 are withdrawn from consideration.

Action Summary

The rejection of claims 1-4, 6 and 8 under 35 U.S.C. 102(b) as being anticipated by Waranis et al. (U.S.Patent No. 5,516,770) is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 1-3 and 5-8 under 35 U.S.C. 102(e) as being anticipated by Rubino et al. (US 2004/0167152 A1) is hereby expressly withdrawn in view of Applicant's amendment.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action as follows:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waranis et al. (U.S.Patent No. 5,516,770) of record in view of Sehgal (EP 0041795 A2) and further in view of Cooperstone et al. (U.S.Patent No. 7,060,709 B2).

Waranis et al. teach an aqueous, injectable rapamycin (also known as sirolimus) solution at a concentration of **0.25mg/ml to 3mg/ml**. (abstract). Waranis et al. illustrate a preparation of rapamycin (sirolimus) at **1mg/ml** with **polyethylene glycol**, **water** and polysorbate. (Examples 2 and 3).

Waranis et al. do not teach the employment of CCI-779 set forth in claim 5, ethanol in a concentration of less than two percent and further comprising Vitamin E TPGS.

Sehgal teaches that the rapamycin composition is prepared by dissolving rapamycin in a nonionic surfactant so that when diluted with water, rapamycin remains in solution. Sehgal teaches that rapamycin is **insoluble** in most surfactants, including nonionic surfactants. Sehgal teaches that nonionic surfactants such as **polyethylene glycol** and **polysorbate** can also be added to the rapamycin composition. (page 7, lines 14-16). Sehgal teaches that the composition is prepared by dissolving rapamycin

in an organic solvent which is capable of dissolving rapamycin and is miscible with the nonionic surfactant such as ethanol, and adding the nonionic surfactant, if required, removing some or all of the organic solvent ,and adding water. (page 6, line 4- page 7, line 5). Sehgal illustrates the preparation of an injectable rapamycin composition by removing ethanol by evaporation. (page 8, example 1).

Copperstone et al. teach that CCI-779 is a rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and can be formulated in an injectable composition. (abstract, column 1, lines 61-67). Cooperstone et al. teach that that use of a surfactant with diluents is advantageous in the CCI-779 parenteral formulation because it prevents precipitation of CCI-779 upon dilution with aqueous infusion solutions or blood. (column 7, lines 7-14).

It would have been obvious to one of ordinary skill in the art to incorporate ethanol in Waranis et al's illustrated rapamycin (sirolimus) formulation comprising **polyethylene glycol**, **water** and polysorbate to first dissolve rapamycin in Waranis et al's formulation because rapamycin is insoluble in most surfactants, including the nonionic surfactants such as **polyethylene glycol** and **polysorbate** contained in Waranis et al's rapamycin formulation. One would have been motivated to first dissolve rapamycin in organic solvent such as ethanol as taught by Sehgal in order to increase the solubility of rapamycin in the formulation. With regard to an ethanol content of less than 2%, such is obvious because Sehgal illustrates removing ethanol by evaporation upon the dissolution of rapamycin in the process of preparing the injectable formulation of rapamycin. Sehgal teaches that some or all of the ethanol content can be removed

once the dissolution of rapamycin takes place. Therefore, the ethanol content of less than 2% is encompassed by the evaporation step taught by Sehgal et al. With regard to the limitation of further comprising vitamin E-TGPS, is obvious because surfactants such as vitamin E-TPGS are advantageous in a rapamycin injectable formulation because they prevents precipitation of rapamycin in that formulation upon dilution as taught by Copperstone et al. One would have been motivated to formulate a rapamycin formulation with additional surfactants such as vitamin E-TPGS in order to prevent precipitation of rapamycin. The employment of CCI-779 is obvious because Copperstone et al. teach that CCI-779 is a rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and can be formulated in an injectable composition.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Response to Arguments

Applicant's arguments filed March 21, 2007 have been fully considered but they are not persuasive. Applicant argues that Waranis et al. do not disclose a liquid formulation comprising rapamycin, ethanol in a concentration of less than two percent, polyethylene glycol and water and, therefore, there is no anticipation. The Examiner is

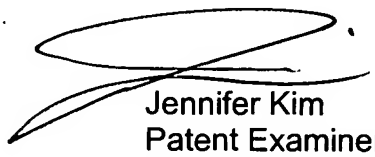
in agreement that Waranis et al. is no longer an anticipatory reference. However, Waranis et al. now qualifies as a reference under 35 U.S.C. 103(a) in view of Sehgal (EP 0041795 A2) and further in view of Cooperstone et al. (U.S.Patent No. 7,060,709B2). (see above rejection). Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Jennifer Kim
Patent Examiner
Art Unit 1617

Jmk
June 11, 2007